62. [unchanged] The polypeptide of claim 34, wherein the polypeptide is enzymatically active.

REMARKS

Applicant has carefully reviewed and considered the Office Action mailed on December 3, 2002, and the references cited therewith.

Claims 34 and 36 are amended; and claim 35 is deleted. As a result, claims 34, 36-48 and 62 are now under examination in this application. Claims 1-33 and 49-61 are withdrawn from consideration in view of the Restriction Requirement.

Support for the amendment to claim 34 can be found throughout the specification, such as original claim 36. Claim 36 has been amended to correct antecedent basis. No new matter has been added.

§103 Rejection of the Claims

Claims 34-35, 37-38 and 47-48 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Schwarze *et al.* (*Science* 285:1569-1572 (1999 Sept 3)) in view of Ghodsi *et al.* (*Exp. Neuro.* 160:109-116, (1999) or *Hum. Gene Therapy* 9:2331-2340 (1998 Nov 1)). Thus, the examiner has inferred that claims 36, 39-46 and 62 are free of the cited art.

Solely for reasons for expediting prosecution Applicant has amended independent claim 34 to recite the features of claim 36. Thus, claim 34 is now recites the features of claim 36, 39, 43 and 45, which the examiner has indicated are free of the cited art. The rejection of the pending claims under 35 U.S.C. § 103(a), therefore, should be withdrawn.

Rejection of the Claims under 35 U.S.C. §112, First Paragraph

Claims 34-48 and 62 were rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for a β-galactosidase fused to a PTD sequence, does not reasonably provide enablement for all types of proteins fused to PTD. As a point of clarification, the examiner on page 3 of the Office Action mailed 12/03/02 used the term "β-galactosidase,"

whereas the working example in the present specification is was to β-glucuronidase (*i.e.*, a lysosomal enzyme).

First, the examiner states on page 3 of the Office Action that one of skill in the art would undergo undue experimentation to practice the invention commensurate in scope to the claims because "the construction of fusion proteins is not a simple task." Applicant respectfully disagrees with the examiner regarding the ease of making fusion proteins. At this point, many kits are commercially available for artisans to easily generate fusion proteins. For example, the Invitrogen, Clonetech and Stratagene companies provide kits for generating fusion proteins. Thus, it is quite routine for artisans to generate fusion proteins. Once the fusion protein is made, the investigator would easily be able to perform a screening assay to test the biological activity of the fusion protein. An investigator wishing to modify a protein with a PTD would know how to assay for its biological activity, or else he or she would not be studying it. Therefore, even if some experimentation was needed in order to test the possible new proteins that would be covered by Applicant's application, it would not require undue experimentation to generate and screen even very large numbers of fusion proteins in view of teaching of the present specification.

Second, the examiner states on pages 3-4 of the Office Action that even if one was successful in generating an enzyme that was functional *in vitro*, one would not know if it was functional *in vivo*. The examiner states that the "expression of a fusion protein in vitro does not confer in vivo success, and as such one of skill in the art would be forced to experiment to determine if the fusion of an enzyme to a PTD would work effectively." The examiner has provided no support for this statement. Applicant asserts that there is no *a priori* reason why a non-denatured protein that has biological activity *in vitro* would no longer have that activity *in vivo*. Applicant is not aware of an example of a non-denatured protein that was biologically active *in vitro*, but no *in vivo*.

Applicant requests that these rejections under 35 U.S.C. § 112, first paragraph, be withdrawn.

Conclusion

Applicant respectfully submits that the claims are in condition for allowance and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney (612-373-6961) to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

BEVERLY L. DAVIDSON ET AL.

By their Representatives,

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. Box 2938
Minneapolis, MN 55402
(612) 373-6961

Date _____ By _____
Ann S. Viksnins
Reg. No. 37,748

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner of Patents, Washington, D.C. 20231, on this _____ day of April, 2003.

Name _____ Signature _____